REMARKS

Claims 1, 3-5, 7, 9-13 and 19-21 remain pending in the present application and have been rejected. Claim 19 is amended herein. Applicants acknowledge the Office's acceptance of the Information Disclosure Statement filed on June 14, 2004.

Objections

The Examiner objected to the abstract as not being descriptive of the invention. A new abstract is submitted herewith. Applicants submit that the objection to the abstract on this basis should be withdrawn.

The Examiner objected to the title of the invention as not being descriptive of the invention. A new title is submitted herewith. Applicants submit that the objection to the title on this basis should be withdrawn.

Claim Rejections under 35 U.S.C. §112, first paragraph

Claims 1, 3-5, 7, 9-13 and 19-21 have been rejected under 35 U.S.C. §112, first paragraph as failing to comply with the written description requirement. More specifically, the Examiner argues that the claims are broadly drawn to a multitude of nucleic acids that hybridize to SEQ ID NO: 1 or to any nucleic acid that encodes SEQ ID NO: 2. The specification, according to the Examiner, only describes a coding sequence from a *Bacillus* species that comprises SEQ ID NO: 1. Furthermore, the Examiner states that no description is provided as to the function of the nucleic acid in claim 1, part c) and the specification also fails to describe signal peptide coding regions and membrane attachment coding regions. Finally, the Examiner argues that the donor

organisms required by the method of claims are not described.

Applicants submit they have satisfied the written description requirement and have reasonably conveyed to one of ordinary skill in the art that applicants had possession of the claimed invention at the time the application was filed. As stated by the Federal Circuit, "an applicant complies with the written description requirement 'by describing the invention, with all its claimed limitations...,'and by using 'such descriptive means as **words** ... that set forth the claimed invention.'" *Lockwood v. Amer. Airlines, Inc., 107 F.3d 1565 (Fed. Cir. 1997)* (emphasis added). In accordance with *Lockwood*, Applicants submit that they have satisfied the written description requirement by using words as its descriptive means. Specifically, Applicants have described the present invention using the terms "nucleic acid," "sequence," "hybridize," and "coding portions." Applicants use these terms in the same manner as they are well known and regularly used in the art.

The Examiner argues that, " the claims are broadly drawn to a multitude of nucleic acids that hybridize to SEQ ID NO: 1 or to any nucleic acid that encodes SEQ ID NO: 2, and describes the specification as only disclosing a coding sequence from a *Bacillus* species that comprises SEQ ID NO:1. We respectfully disagree. The claims are drawn to a) a nucleic acid having the sequence of the coding portion of SEQ ID NO: 1, which is fully described in the specification; b) a nucleic acid encoding the amino acid sequence of SEQ ID NO:2, which again is fully described in the specification and c) a nucleic acid molecule that hybridizes to the coding portion of SEQ ID NO:1 or to any nucleic acid encoding the amino acid of SEQ ID NO:2. Given the well-known

base-pairing complementarity, one would immediately discern a multitude of sequences with the scope of claim 1(c). Furthermore, the specification starting on page 11, describes the present invention as providing a new strategy for engineering resistance to and treatment of disease, which targets N-acyl homoserine lactone autoinducers used by pathogens. While the invention is exemplified with reference to the aiiA gene and protein, one would readily understand, from the present disclosure, the applicability of the invention to other such proteins whether they are aiiA homologs or not. The present specification, especially the examples, describe the techniques, screens, *etc.* needed to extend the invention beyond the specific aiiA protein. A person skilled in the art would be capable of identifying genes that encode autoinducer inactivator proteins as claimed based on the information provided in the specification.

Accordingly, it is submitted that the specification provides an adequate written description of the claimed invention. Withdrawal of this rejection is requested.

The Examiner argues that no description is provided as to the function of the nucleic acid in claim 1 part c). Claim 1 part c), claims a nucleic acid that either hybridizes to a nucleic acid having the sequence of the coding portion of the aiiA gene or hybridizes to a nucleic acid encoding the amino acid sequence of the aiiA gene product. The function is that c) hybridizes to a) and b). The resulting nucleic acid molecule then may be used to confer bacterial resistance in plants or animals or can be introduced into a cell such that the inactivation protein is expressed by the plant or animal. *See* pages 9-10. The resulting nucleic acid molecule also has the effect of reducing or eliminating the activity of bacterial autoinducers. *Id.* Consequently, the protein, and

any nucleic acid that encodes the protein, may be used to reduce or eliminate the effect of such bacteria. *Id.*

Accordingly, it is submitted that the specification provides an adequate written description of the claimed invention. Withdrawal of this rejection is requested.

One of skill in the art also understands that signal peptide coding regions are well known in the art. The Examiner argues that the specification fails to describe signal peptide regions and membrane-attachment regions. We respectfully disagree. The specification discloses at page 9 that the nucleic acid optionally may further comprise a signal peptide coding region. It is fundamental biology that signal peptides are about 20 amino acids and mark polypeptides of proteins destined for secretion. It is a peptide present on proteins that are destined either to be secreted or to be membrane components. It is usually at the N terminus and normally absent from the mature protein. *See Biology: Sixth Edition:* 320 (2002). At page 10 of the specification, lines 25-31 describe pathogenic bacteria cells as confined to the intercellular area of plant tissue. Since it is desirable to target the aiiA protein into the intercellular spaces, a secretion signal peptide may be fused to the aiiA protein in order to accomplish this. The specification also discloses four references at lines 30-31 that describe such a process.

Accordingly, it is submitted that the specification provides an adequate written description of the claimed invention. Withdrawal of this rejection is requested.

Membrane attachment coding regions are also described in the specification. At pages 10-11 of the specification, lines 31-32 describe a plant membrane attachment motif as something

that can be incorporated into the peptide sequence of AiiA for anchoring the AiiA enzyme in the outer surface of plant cell membranes.

Accordingly, it is submitted that the specification provides an adequate written description of the claimed invention. Withdrawal of this rejection is requested.

Finally, the Examiner argues that the donor organisms provided by the method of the claims are not described. Bacterial isolates from plant and soil samples were screened for enzymatic inactivation of AIs (*i.e.*, bacterial isolate 240B1) and are disclosed at page 15 of the specification. Withdrawal of this rejection is requested.

Claims 1, 3-5, 7, 9-13 and 19-21 are rejected under 35 U.S.C. §112, first paragraph, because the Examiner reasons that the specification while being enabling for nucleic acids encoding SEQ ID NO: 2, does not reasonably provide enablement for nucleic acids that hybridize to SEQ ID NO: 1 or that hybridize to any nucleic acid that encodes SEQ ID NO: 2, vectors comprising them, cells transformed with the vector and a method of using the nucleic acids to increase disease resistance in a plant.

The Examiner also argues that the instant specification fails to provide guidance for which amino acids of SEQ ID NO:2 can be altered and to which amino acids must not be changed to maintain lactonase activity of the encoded protein. The specification, according to the Examiner, fails to provide guidance for which amino acids can be deleted and which regions of the protein can tolerate insertions and still produce a functional enzyme. Therefore, it would be undue experimentation to "evaluate nucleic acids that hybridize to SEQ ID NO:1 or that

hybridize to any nucleic acid that encodes SEQ ID NO:2." As stated above, the amended claims are drawn to a) a nucleic acid having the sequence of the coding portion of SEQ ID NO: 1; b) a nucleic acid encoding the amino acid sequence of SEQ ID NO:2; and c) a nucleic acid molecule that hybridizes to the coding portion of SEQ ID NO:1 or to any nucleic acid encoding the amino acid of SEQ ID NO:2 wherein said nucleic acid of c) encodes a bacterial autoinducer inactivation protein.

To satisfy the enablement requirement, the specification must teach those of skill in the art how to make and use the entire scope of the ***claimed*** invention without undue experimentation (emphasis added). *Genentech, Inc. V. Novo Nordisk, A/S*, 42 U.S.P.Q.2d 101, 1004 (Fed. Cir. 1997), *cert. denied*, 522 U.S. 963 (1997). The specification need not disclose what is well-known to those skilled in the art and preferably omits that which is well-known and already available to the public. M.P.E.P. 2164.05(a); *Spectra-Physics, Inc. V. Coherent, Inc.*, 3 U.S.P.Q.2d 1737, 1743 (Fed. Cir. 1987), *cert. denied*, 484 U.S. 954 (1987). Applicants are not required to provided detailed information concerning matters which are known in the prior art and well within the ordinary skill of a practitioner. *See* M.P.E.P. 2164.05(a). Even if the specification requires the skilled person in the art to engage in a "reasonable" amount of routing experimentation, the specification complies with the enablement requirement so long as such experiment is not "undue." *In re Wands*, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988). A patent application is presumptively enabled when filed. *E.g., In re Marzocchi,* 169 U.S.P.Q. 367, 370 (C.C.P.A. 1971). "A specification that teaches how to make and use the invention in terms

which correspond in scope to the claims must be taken as complying with the first paragraph of 35 U.S.C. 112 unless there is reason to doubt the objective truth of the statements relied upon therein for enabling support." *Id.*

The "examiner has the initial burden to establish a reasonable basis to question the enablement provided for the **claimed** invention." M.P.E.P. 2164.04; *In re Wright*, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir. 1993) (emphasis added). In *Wright*, the Court made clear that the PTO has the burden of providing a reasonable explanation of why the specification does not enable. If the examiner is able to provide such evidence or reasoning, she has established a *prima facie* case of nonenablement. *See* M.P.E.P. 2164.04. As the Court said in *Marzochi*,

> [I]t is incumbent upon the Patent Office, whenever a rejection on this basis [i.e. doubt of the objective truth of statements in the specification] is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertion of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go through the trouble and expense for supporting his presumptively accurate disclosure.

169 U.S.P.Q. at 370.

One of skill in the art knows that nucleic acid hybridization is a process where the nucleic acid base pairs with a complimentary sequence of another nucleic acid molecule. The temperature and salt concentrations at which hybridization is performed has a direct effect upon the results that are obtained. Specifically, you can set the conditions up so that your hybridizations only occur between the probe and a filter bound nucleic acid that is highly homologous to that probe. Therefore, one of skill in the art would know that the nucleic acid of

part c) would base pair to either the nucleic acid having the sequence of the coding portion of SEQ ID NO: 1 or the nucleic acid encoding the amino acid sequence of SEQ ID NO: 2. Both sequences for SEQ ID NO: 1 and SEQ ID NO: 2 are disclosed in Figures 4(a) and 4(b).

The hybridization conditions in part c) of claim 1 are designed to hybridize aiiA derivatives with more than 80% (Eff Tm of aiiA) homology at the DNA sequence level. One of skill in the art could easily perform such a calculation based on a standard formula provided at the website:

http://www.ndsu.nodak.edu/instruct/mcclean/plsc731/dna/dna6.htm

Standard Formula

Eff T_m=81.5+16.6(log M [Na+])+0.41(%G+C)

As aiiA=37% GC, 1XSSC[Na+]M=0.165, then

Eff T_m of aiiA= 81.5+16.6(log 0.165)+0.41 (37%) =81.5-13+15.17=83.5.

Since it has been well established that a 1% mismatch of two DNA molecules lowers the T_m 1.4°C, when temperature of hybridization is at 55° C, the minimum homology of the DNA target to the probe (aiiA) can be calculated using 83.5% from the calculation above:

% Homology=100-[(83.5-55)/1.4]=100-20.36=79.6%

As a result, the conditions stated in part c) of claim 1 are stringent to ensure hybridization of aiiA derivatives with high homologies (>79%).

Applicants submit that the Examiner has not provided acceptable evidence to doubt the objective enablement of the specification and to support her contention that the specification is

not enabling. Accordingly, it is submitted that the specification provides enablement for the claimed invention. Withdrawal of this rejection is requested.

According to the Examiner, the specification does not teach under which promoters the nucleic acid that hybridizes to SEQ ID NO:1 or that hybridizes to any nucleic acid that encodes SEQ ID NO:2 must be expressed from in plants to provide disease resistance. It is well known in the art that the DNA sequence where RNA polymerase attaches and initiates transcription is known as the promoter. The promoter of a gene includes within it the transcription start point and typically extends several dozen nucleotide pairs "upstream" from the start point. One skilled in the art with the aid of a computer can locate promoters by inspection of the nucleotide sequence. At page 10, the specification describes the sequence being introduced into plant or animal cells by well-known methods. *E. coli* promoters are characterized by two sequences, the -35 sequence and the -10 sequence (Pribnow box) named for their approximate location relative to the start point of transcription. Centered 10 base pairs upstream of the start-point of transcription, this sequence element has the consensus sequence TATAAT. At page 17 of the specification, there is discussion of a sequence match to the consensus -10 promoter element (TATAAT) that occurs 35 bp upstream of the initiation codon. One can even compare a number of promoters and determine the frequencies of the four nucleotides at each position in the -35 to -10 sequences. Over the years, a number of authors have compiled lists of *E. coli* promoters and analyzed their sequences. From these the original consensus sequence elements and sequences have been confirmed. Therefore one of skill in the art with the aid of the specification could

locate the promoters using well known molecular biology techniques.

Accordingly, it is submitted that the specification provides enablement for the claimed invention. Withdrawal of this rejection is requested.

The Examiner argues that the specification allegedly does not describe the transformation of any plant with a nucleic acid that hybridizes to SEQ ID NO:1 or that hybridizes to any nucleic acid that encodes SEQ ID NO:2; therefore, it would be undue trial and error to screen through the myriad of nucleic acids encompassed by the claims and plants transformed therewith, to identify those with increased disease resistance, if such plants are even obtainable. However, in *In re Borkowski*, 164 U.S.P.Q. 642, 645 (C.C.P.A. 1970), the court reasoned that a specification need not even contain a single working example to be considered enabling. Even so, the present invention relates to a method for increasing disease resistance in a plant or animal, by introducing into the cell of the plant or animal a nucleic acid sequence which encodes a bacterial autoinducer inactivation protein in a manner which allows the cell to express the nucleic acid sequence. *See* page 5, lines 18-24. It would not be undue trial and error to screen through the nucleic acids encompassed by the claims because the nucleic acid that hybridizes to SEQ ID NO:1 or that hybridizes to a nucleic acid encoding SEQ ID NO:2 is a nucleic acid that encodes a bacterial autoinducer inactivation protein. The specification also identifies plants with increased disease resistance. Diseases of various plants including potato, cabbages, tomato, chili, carrot, celery, onion, and lettuce are known in the art. *See* pages 19-20. Any molecular biologist of ordinary skill can easily identify the nucleic acids encompassed by the claims and utilize well-known

hybridization techniques to transform a diseased plant.

Accordingly, it is submitted that the specification provides enablement for the claimed invention. Withdrawal of this rejection is requested.

The specification, according to the Examiner does not teach from which organisms the nucleic acid of claim 1, part c) can be isolated, or which organisms can be used as donor organisms in the method of claims 19-21, and also argued that bacterial isolate 240B1 cannot be used to isolate the nucleic acid of SEQ ID NO:1 because it is not deposited or publicly available. The Examiner also argues that the specification does not describe the isolation of a nucleic acid that hybridizes to SEQ ID NO:1 or that hybridizes to any nucleic acid that encodes SEQ ID NO:2 from a publicly available donor organism, and undue trial and error experimentation would be required to screen all the donor organisms encompassed by the claims to identify those that have a nucleic acid that hybridizes to SEQ ID NO:1 or that hybridizes to any nucleic acid that encodes SEQ ID NO:2.

The sequence with accession number AF196486 from *Bacillus* sp. 240B1 is publicly available in GenBank and references such as *Nature Biotechnology*, Vol. 19: 735-736 (2001) and *Proc. Natl Acad Sci,* Vol. 7: 3526-3531(2000), although it need not be made publicly available due to its disclosure in the specification. It would not be undue trial and error experimentation to isolate a nucleic acid that hybridizes to SEQ ID NO:1 or that hybridizes to any nucleic acid that encodes SEQ ID NO:2 from a publicly available donor organism, because *Bacillus* sp. 240B1 is publicly available. Even so, it would be reasonable using standard molecular biology techniques

and a computer to screen for soil isolates for acyl homoserine lactone degrading activity.

Accordingly, it is submitted that the specification provides enablement for the claimed invention. Withdrawal of this rejection is requested.

Claim Rejections under 35 U.S.C. §112, second paragraph

Claims 1, 3-5 and 19-21 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicants regard as the invention. More specifically, claim 1, according to the Examiner is indefinite in its recitation of "the coding portion of SEQ ID NO: 1" in part (a). The Examiner argues that any nucleic acid has at least 6 potential reading frames, and thus at least 6 coding portions. Applicants respectfully disagree. Those skilled in the art would understand the scope of the claim when the claim is read in light of the specification. *North American Vaccine Inc. v. American Cyanamide Co.*, 28 USPQ2d 1333, 1339 (Fed. Cir. 1993)(citing *Orthokinetics, Inc. v. Safety Travel Chairs,* 1 USPQ.2d 1081, 1088 (Fed. Cir. 1986)) *cert. denied*, 511 US. 1069 (1994). Figure 4A shows the nucleotide sequence of the aiiA gene [SEQ ID NO: 1]. The specification discloses the coding portion as starting at base 1. Bases 1-3 in Figure 4 stand for the DNA codon ATG which one of skill in the art knows is the mRNA start codon AUG. The termination site is labeled by a thick underline *See* page 7, lines 27-30. Claim 1 part (a) distinctly claims the coding portion of SEQ ID NO: 1.

For the above reasons, Applicants respectfully submit that the claims distinctly claim the

subject matter of the present invention and request that the rejection under 35 U.S.C. §112, second paragraph be withdrawn.

In view of the above amendments and remarks, it is submitted that the claims are in condition for allowance. The Examiner is invited to telephone the undersigned to expedite allowance of this application.

RESPECTFULLY SUBMITTED,			
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